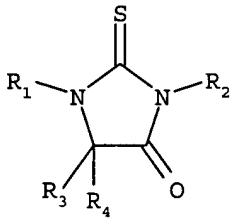
10/529817
JC17 Rec'd PCT/PTO 31 MAR 2005

Amendments to the Specification:

Please make the following correction to the paragraph beginning at page 2, line 17:

According to the invention, novel compounds are proposed that contain the 2-~~thioxoimidazolin-4-one~~ thioxoimidazolidin-4-one (or 2-thiohydantoin) ring and are selected from:

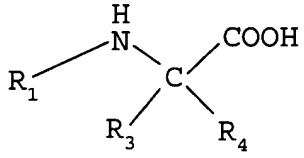
a) compounds of the formula



(I)

Please make the following correction to the paragraph beginning at page 12, line 10:

~~1)~~ a) reacting an acid of the formula



(II)

in which R_1 is as defined above for the compounds of formula (I), R_3 is H, C_1-C_4 alkyl, phenyl or benzyl and R_4 is H or alkyl,
with an isothiocyanate of the formula

$$R_2\text{-}N{=}C{=}S \qquad \text{(III)}$$

in which R_2 is a group as defined above for the compounds of formula (I), in a solvent such as ethanol, at a temperature between 20°C and the boiling point of the solvent, in the presence of an aprotic base such as triethylamine, for 1 to 20 hours, to give the compound of formula (I):

Please make the following 2 corrections to the paragraph beginning at page 14, line 31:

In these Examples, "Preparation" denotes those which describe the synthesis of intermediates, and ~~"Examples"~~ "Example" denotes those which describe the synthesis of compounds of formula (I) according to the invention. The melting points are measured on a ~~Kofler~~ Koffler bench and the nuclear magnetic resonance spectral values are characterized by the chemical shift calculated relative to TMS, by the number of protons associated with the signal and by the shape of the signal (s for singlet, d for doublet, t for triplet, q for quadruplet, m for multiplet). The operating frequency and the solvent used are indicated for each compound.

Please make the following correction to the paragraph beginning at page 19, line 1:

PREPARATION XIV

N-[(4-phenoxyphenyl)methyl]alanine ethyl ester

A procedure analogous to that of Preparation VII is followed, except that 4-phenoxybenzenemethanamine and ethyl 2-bromopropionate are used as the ~~starting material~~ starting materials in dioxane, to give the expected product in the form of a beige oil (yield = 37%).

^{1}H NMR (300 MHz, DMSO): 7.37 (m, 4H); 7.12 (t, 1H); 6.97 (m, 4H); 4.09 (q, 2H); 3.63 (2d, 2H); 3.24 (q, 1H); 1.20 (m, 6H).

Please make the following correction to the paragraph beginning at page 23, line 18:

PREPARATION XXXIII

1-Isothiocyanato-4-(phenylmethyl)benzene

A solution of 5 g (27 mmol) of 4-(phenylmethyl)aniline in 20 ml of dimethylformamide is prepared and a solution of ~~5.77 g~~ 5.17g (29 mmol) of 1,1'-thiocarbonyldiimidazole in 20 ml of dimethylformamide is added at 0°C, with stirring. The reaction medium is stirred for 5 h at 5°C and then poured into iced water. The mixture obtained is extracted twice with 100 ml of dichloromethane and the combined organic phases are washed with water and then dried over sodium sulfate and concentrated under reduced pressure. The residue is purified by chromatography using cyclohexane as the eluent to give the expected product in the form of an oil, which crystallizes in the refrigerator (yield = 88%).

M.p. < 50°C

Please make the following correction to the paragraph beginning at page 32, line 16:

Example 28 a

5-Methyl-1-(4-phenoxyphenyl)- ~~3-(pyridinyl)~~ 3-(pyridin-3-yl) -2-thioxoimidazolidin-4-one

A procedure analogous to that of Example 19 is followed, except that pyridin-3-yl isothiocyanate is used as the starting material, to give the expected product in the form of a white foam (yield = 68%).

^{1}H NMR (300 MHz, DMSO): 8.63 (m, 2H); 7.88 (m, 1H); 7.50 (2m, 5H); 7.17 (2m, 5H); 5.07 (q, 1H); 1.39 (d, 3H).

Please make the following correction to the paragraph beginning at page 32, line 23:

Example 28 b

5-Methyl-1-(4-phenoxyphenyl)- ~~3-(pyridinyl)~~ 3-(pyridin-3-yl) -2-thioxoimidazolidin-4-one hydrochloride

A procedure analogous to that of Example 26 b is followed, except that the compound obtained according to Example 28 a is used as the starting material, to give the expected product in the form of white crystals (yield = 96%).

M.p. = 140°C

Please make the following correction to the paragraph beginning at page 34, line 12:

Example 35

1-(4-Phenoxyphenyl)-3-phenyl-5-phenylmethyl-2-thioxoimidazolidin-4-one

A procedure analogous to that of Example 19 is followed, except that the acid obtained according to Preparation IX and phenyl isothiocyanate are used as the ~~starting material~~ starting materials, to give the expected product in the form of a fine white solid (yield = 30%).

M.p. = 130°C

Please make the following correction to the paragraph beginning at page 35, line 7:

Example 39

1-[4-(2-Chlorophenoxy)phenyl]-5-methyl-3-phenyl-2-thioxoimidazolidin-4-one

A procedure analogous to that of Example 19 is followed, except that the compound obtained according to Preparation XII and phenyl isothiocyanate are used as the ~~starting material~~ starting materials, to give the expected product in the form of a white powder (yield = 25%).
M.p. = 108°C

Please make the following correction to the paragraph beginning at page 36, line 26:

Example 44

5-Methyl-3-(4-phenoxyphenyl)-1-phenylmethyl-2-thioxoimidazolidin-4-one

A procedure analogous to that of Example 19 is followed, except that N-(phenylmethyl)alanine and 4-phenoxyphenyl isothiocyanate are used as the ~~starting material~~ starting materials, to give the expected product in the form of an off-white powder (yield = 50%).
M.p. = 138°C

Please make the following correction to the paragraph beginning at page 37, line 8:

Example 46

3-(4-Nitrophenyl)-1-(4-phenoxyphenyl)-2-thioxoimidazolidin-4-on

A procedure analogous to that of Example 19 is followed, except that N-(4-phenoxyphenyl)glycine and 4-nitrophenyl isothiocyanate are used as the ~~starting material~~ starting materials, to give the expected product in the form of a beige powder (yield = 40%).

M.p. = 204°C

Please make the following correction to the paragraph beginning at page 50, line 19:

Example 138

5-Methyl-1-[4-(phenylmethoxy)phenyl]-3-(2-propenyl)-2-thioxoimidazolidin-4-one

A mixture of 0.6 g (2.2 mmol) of the acid obtained according to Preparation XXVI and 18 ml of acetonitrile is prepared. 0.5 ml ~~(3.7 ml)~~ (3.7 mmol) of triethylamine is added (giving a solution), followed by 0.325 ml (3.3 mmol) of allyl isothiocyanate. The reaction mixture is stirred for 15 h at room temperature and the solvent is then removed under reduced pressure. The residue is purified by chromatography on silica gel using a cyclohexane/ethyl acetate mixture (9/1; v/v) as the eluent to give 0.73 g of the expected product in the form of a white solid (yield = 93%).

M.p. = 88-90°C

Please make the following 2 corrections to the paragraph beginning at page 61, line 19:

Example 190

3-[4-(Phenylmethyl)phenyl]-1-(2-propenyl)-2-thioxoimidazolidin-4-one

A solution of ~~2.40~~ 0.24g (2 mmol) of the ethyl ester of ~~N-alkylglycine~~ N-allyl glycine in 25 ml of toluene is prepared and 0.5 g (2.2 mmol) of the isothiocyanate obtained according to Preparation XXXIII and 2.2 ml of acetic acid are added. The reaction mixture is heated gently at the reflux temperature of the solvent for 2 hours, with stirring, and then concentrated under reduced pressure. The residue is purified by chromatography on silica gel using dichloromethane as the eluent to give the expected product in the form of a beige powder (yield = 65%).

M.p. = 108°C

Please make the following correction to the paragraph beginning at page 63, line 8:

Example 198

1-(4-Chlorophenyl)-3-[4-(phenylmethyl)phenyl]-2-thioxoimidazolidin-4-one

A procedure analogous to that of Example 197 is followed, except that the ethyl ester of N-(4-chlorophenyl)glycine is used as the ~~starting material~~ starting materials, to give the expected product in the form of orange crystals (yield = 63%).

M.p.=153°C